the West might be to the scenarios described in New York City and what can be done to prevent similar public health disasters here.

In 1994 the Centers for Disease Control and Prevention published findings of a national survey of drug-resistant TB in the United States. During the first three months of 1991, a total of 3,256 cases were identified that were tested to both isoniazid and rifampin, and 114 (3.5%) of these were resistant to both drugs. Of 64 cities with populations over 250,000, 7 reported multidrug-resistant TB cases, and although the highest resistance rate was in New York City (13.9%), three California cities—Oakland, Sacramento, and Los Angeles—were included. Los Angeles is the most populous California city on the list, and the county of Los Angeles is even larger, containing more than 9 million people (more than 42 entire states). Nevertheless, of 1,622 new TB cases reported from Los Angeles County (excluding Pasadena and Long Beach) in 1995, only 20 (1.2%) had multidrug-resistant TB (TB Control, Los Angeles County, provisional data), and the resistance rate continues to be far below that of New York City. The factors that are thought to have contributed to the development of multidrug-resistant TB and subsequent outbreaks are all present in Los Angeles County, including homelessness, immigration, substance abuse, nonadherence to drug regimens, and an HIV epidemic. Why isn't multidrug-resistant TB more common, and what can we do to prevent future outbreaks?

Since 1985, the Los Angeles County Health Department has used Rifamate (Marion Merrell Dow), a fixed-dose combination antituberculosis medication containing both isoniazid and rifampin. The use of this formulation may partly explain the low rates of multidrug-resistant TB in this county because it prevents patients from taking either drug alone, thus decreasing the risk of drug resistance developing from unintended monotherapy. The use of Rifater (Marion Merrell Dow), a fixed-dose preparation containing isoniazid, rifampin, and pyrazinamide, should also be considered when starting patients on empiric treatment pending susceptibility results.

Drug resistance is also prevented by interventions such as directly observed therapy that increases patient adherence to and completion of treatment. Incentives may do the same. In Los Angeles County, the percentage of homeless patients in the Skid Row area completing treatment was 53% in 1987. But by 1994, about five years after the creation of a food-and-housing incentive program, this had increased to 96%.

Finally, rapid and accurate clinical diagnosis shortens the duration of infectiousness by ensuring prompt treatment with appropriate medications. This is especially important in persons with the acquired immunodeficiency syndrome, whose symptoms may be attributed to *Mycobacterium avium* complex when *Mycobacterium tuberculosis* is the real culprit. Obtaining specimens for culture confirmation and susceptibility testing, preferably before starting an antimycobacterial drug regimen, is critical in this population, as is ruling out active TB before starting preventive therapy.

Public health interventions must be aggressively applied because the factors for multidrug-resistant TB outbreaks are all present in Los Angeles, and New York City is much closer than we think.

ANNETTE NITTA, MD
Los Angeles, California

REFERENCES

Bloch AB, Cauthen GM, Onorato IM, et al: Nationwide survey of drug-resistant tuberculosis in the United States. JAMA 1994; 271:665–671

Dooley SW, Jarvis WR, Martone WJ, Snider DE Jr: Multidrug-resistant tuberculosis (Editorial). Ann Intern Med 1992; 117:257–259

Iseman MD: Treatment of multidrug-resistant tuberculosis. N Engl J Med 1993; 329:784–791

Moulding T, Dutt AK, Reichman LB: Fixed-dose combinations of antituberculous medications to prevent drug resistance. Ann Intern Med 1995; 122: 951–954

Smoking Cessation—New Challenge and Opportunities

THE NEED FOR and means of assistance with smoking cessation have seldom been greater than in 1996. Increasingly, both the adverse effects of smoking and the availability of effective means of assisting smoking cessation are clear. Increases in both the strength and range of smoking-related risks have been noted since the 1960s. Smoking-cessation behavioral and pharmacotherapies are rapidly increasing in availability and ease of use.

Pharmacotherapies for stopping smoking now include nicotine (polacrilex) gum, patches, and nasal spray; the first two have recently become available over the counter in drugstores. Antidepressants are increasingly being investigated as an aid to stopping smoking, with the use of bupropion hydrochloride showing the most promise to date.

The availability of smoking-cessation aids is dramatically increasing. Inexpensive or free outbound phone counseling such as the multilingual California Smokers' Helpline (1-800-7NO-BUTTs) or insurer or private phone services are widely, promptly, and conveniently available. Federal (Agency for Health Care Policy and Research) guidelines on smoking cessation assistance are free by calling 1-800-358-9295.

Highly concentrated smoking-related risks exist in continuing smokers and are amenable to intervention in physicians' offices. The "Ask, Advise, Assist, and Arrange" model of smoking-cessation assistance is recommended. Clinicians are encouraged to ask about their patients' smoking status. Physicians should advise smokers of smoking's risks and the benefits of stopping. Assisting patients by providing them pamphlets, nicotine replacement, or referrals to phone, class, or other smoking-cessation resources increases quit rates. Arrangements for follow-up are important to support patients' smoking-cessation efforts.

BRUCE N. LEISTIKOW, MD, MS
Davis, California

REFERENCES

DiFranza JR, Lew RA: Effect of maternal cigarette smoking on pregnancy complications and sudden infant death syndrome. J Fam Pract 1995; 40:385–394

Ferry L, Burchette R: Efficacy of bupropion for smoking cessation in non-depressed smokers (Abstr). J Addict Dis 1994; 13:249 [abstract 9A]

Law M, Tang JL: An analysis of the effectiveness of interventions intended to help people stop smoking. Arch Intern Med 1995; 155:1933–1941

Thun MJ, Day-Lally CA, Calle EE, et al: Excess mortality among cigarette smokers: Changes in a 20-year interval. Am J Public Health 1995; 85:1223–1230

Naltrexone Hydrochloride Use in the Treatment of Alcoholism

ALCOHOLISM IS a primary chronic disease with genetic, psychosocial, and environmental factors influencing its development and manifestations. The disease is often progressive and fatal. It is characterized by impaired control over drinking, preoccupation with the drug alcohol, the use of alcohol despite adverse consequences, and distortions in thinking, mostly denial. It is one of the most pervasive medical and social problems of our time. Not surprisingly, the treatment of alcoholism is also one of the most elusive, not only of this generation but since civilizations have been crushing grapes to make wine.

To date, the treatment of alcoholism has largely been characterized by detoxification and referral to various rehabilitation programs—12-step groups, recovery homes, church, and psychotherapy. Disulfiram (Antabuse), which blocks the metabolism of alcohol, produces a possibly toxic reaction with noxious effects that include nausea, vomiting, headache, and facial flushing. Although it has been available for many years, its efficacy has been shown only in patients who are willing to take the medication daily and are participating in a rehabilitation program.

The development of naltrexone hydrochloride as a pharmacologic adjunct to the treatment of alcoholism was based initially on studies using animals that looked at excessive alcohol consumption. It was found that alcohol-preferring strains of mice and rats have increased basal β-endorphin levels in the pituitary gland and in some brain areas relative to alcohol-nonpreferring rats. When alcohol-preferring rats were given naltrexone hydrochloride, a pure opioid antagonist, alcohol consumption decreased. In humans, nonalcoholic persons with a strong family history of alcoholism (high risk) were compared with nonalcoholic persons with no family history of alcoholism (low risk). Baseline plasma β-endorphin levels were lower in the high-risk group, and a small dose of alcohol caused a substantially greater increase in plasma β-endorphin levels than in those of the low-risk group. Based on these and other studies, the endogenous opioid hypothesis was formulated that proposes that the ingestion of alcohol stimulates the release of endogenous opioids that increase some of the rewarding effects of alcohol. This is not to say that endorphins are the only neurotransmitter involved in the behavior associated with alcohol consumption; serotonin and dopamine have also been implicated, and clearly there are multiple mechanisms that need further study.

What has been shown in other studies is that naltrexone hydrochloride use does seem to reduce craving, the relapse rate, and the "high" associated with alcohol consumption when combined with some form of psychological or social therapy. Studies were conducted using patients from the Philadelphia (Pennsylvania) Veterans Affairs Medical Center who had 20 years or more of heavy alcohol use; met 5 of 9 criteria of the *Diagnostic and Statistical Manual of Mental Disorders*, third edition, revised, for alcohol dependence; and did not have a major psychiatric illness. During the 12-week period when patients received naltrexone hydrochloride, 50 mg per day, versus placebo, the placebo-treated group met criteria for relapse in 54% of cases, but the drug-treated group met criteria in only 23% of cases. Relapse criteria included drinking five or more days within a week, five or more drinks per drinking episode, or coming to the clinic with a blood alcohol level of higher than 22 nmol per liter (100 mg per dl).

Clearly it could be argued that the accepted standard of care or the treatment goal in alcoholic patients is total abstinence. Naltrexone use seems to reduce the risk of relapse but does not prevent a person with alcoholism from picking up the first drink. Thus, naltrexone may be most effective in patients with a higher risk for relapse—that is, patients with greater somatic symptoms and higher levels of alcohol craving, when accompanied by some form of behavioral or social therapy.

STEVEN R. EY, MD
Corona Del Mar, California

REFERENCES

Gianoulakis C: Endogenous opioids and excessive alcohol consumption. J Psychiatry Neurosci 1993; 18:148–156

Hyman SE: A man with alcoholism and HIV infection. JAMA 1995; 274:837–846

Swift RM: Effect of naltrexone on human alcohol consumption. J Clin Psychiatry 1995; 56(suppl 7):24–29

Volpicelli JR, Alterman AI, Hayashida M, O'Brien CP: Naltrexone in the treatment of alcohol dependence. Arch Gen Psychiatry 1992; 49:876–880